## REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

## I. CLAIM STATUS & AMENDMENTS

Claims 1-5, 7, 9-14 and 21-26 were pending in this application when last examined and stand rejected.

Claim 1 is amended to recite "wherein the test protein does not directly interact with the organelle-targeting signal peptide of the fusion peptide (a)". Support for this amendment can be found in Figures 1 and 10 as well as throughout the specification as filed.

Claim 21 is amended to clarify the claimed invention in order to expedite prosecution.

Claim 9 is amended to correct a typographical error.

Claims 23-26 are cancelled without prejudice or disclaimer thereto.

No new matter has been added.

## II. DOUBLE PATENTING OBJECTION

On page 3, the Office indicates that if claims 11-14 are found allowable, new claims 23-26 will be objected to as being substantial duplicates thereof. These claims are cancelled and therefore this concern is moot.

## III. NONSTATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION

On pages 3-4 of the Office Action, claims 1-5, 7, 9-14 and 21-26 were rejected on the ground of nonstatutory obvious-type double patenting as being unpatentable over claims 1, 2 and 4-8 of US Patent No. 7,166,447 in view of Ozawa et al., Hamilton et al., Simpson et al., and Martoglio et al.

Without intending to acquiesce to this rejection and merely to expedite allowance of the application, the Applicants submit herewith a Terminal Disclaimer under 37 CFR 1.321, which is signed by a registered attorney of record, together with the fee required under 37 CFR 1.20(d) to

overcome the obviousness-type double patenting rejection over claims 1, 2 and 4-8 of US Patent No. 7,166,447 in view of the noted references. The Terminal Disclaimer removes this patent as a reference.

Therefore, this double patenting rejection is untenable and should be withdrawn.

## IV. OBVIOUSNESS REJECTION

On page 4, claims 1-5, 7, 9-14 and 21-26 were rejected under 35 U.S.C. 103(a) as obvious over Umezawa et al. as applied to claim 6, 8, 17 and 19 in further view of Ozawa et al., Hamilton et al., Simpson et al. and Martoglio et al.

Applicants respectfully traverse this rejection, as applied to the amended and remaining claims. Applicants note that claims 23-26 have been cancelled and therefore this rejection with regard to these claims is moot. Applicants further note that the above-mentioned Terminal Disclaimer does not indicate that the Applicants admit to the appropriateness of this rejection.

As noted in our last response, the probe for protein-protein interaction disclosed in Umezawa et al. and Ozawa et al. utilize protein splicing upon direct interaction of target protein A with target protein B, which are fused in probe (a) and probe(b), respectively. In other words, through direct interaction of protein A and protein B, probe (a) and probe (b) also directly interact for the protein splicing.

On the other hand, the organelle-targeting signal (OTS) peptide of fusion peptide (a) and the test protein of fusion peptide (b) of the present invention **do not directly** interact. Such is made clear by amended claim 1. The protein splicing occurs only when the OTS peptide and the test protein are individually co-localized in the same organelle. That is, the interaction between fusion peptide (a) and fusion peptide (b) for protein splicing occurs through an **indirect manner**, since the organelle lies between them. The cited references fail to disclose or suggest this element of the amended claims.

Applicants note that the Office was unconvinced by such arguments. In particular, the Office notes that if the interaction between fusion peptides (a) and (b) is indirect, such is not recited in the claims. Applicants note that such is now recited in claim 1.

Further, the Office notes that it is unclear why the skilled artisan would expect the fusion proteins to interact via the targeting signal domains. Applicants note that claim 1, as amended, clarifies that fusion peptides (a) and (b) do not interact via the targeting signal domains. Instead, proteins splicing for signal emission occurs when fusion proteins (a) and (b) are in close proximity at the surface of target organelle.

Finally, the Office notes that it is unclear how the two fusion proteins, if they are separated by an organelle membrane, could interact and generate a fluorescent signal.

This is an inventive concept of this application. Close proximity of the two fusion peptides is sufficient for protein splicing to generate the fluorescent signal. Proximity happens when:

(i) Fusion peptide (a) is localized at an organelle by the action of organelle-targeting signal peptide; and

(ii) Fusion peptide (b) is also localized at the same organelle when the test protein is an organelle-localized protein.

For these reasons, Applicants respectfully submit that the present invention is novel and non-obvious over the cited references, because protein splicing for signal emission occurs even if the interaction between fusion peptide (a) and fusion peptide (b) is **indirect**. The cited references fail to disclose or suggest this and therefore do not render obvious the present invention.

Thus, Applicants respectfully suggest that this rejection is untenable and should be withdrawn.

## CONCLUSION

In view of the foregoing amendments and remarks, the present application is in condition for allowance and notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned at the telephone number below.

Respectfully submitted,

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